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<input type="checkbox"/>	L12	L10 and L11	9
<input type="checkbox"/>	L11	methotrexate.clm.	1242
<input type="checkbox"/>	L10	L8 and L9	127
<input type="checkbox"/>	L9	pain.clm.	6944
<input type="checkbox"/>	L8	L6 and L7	247
<input type="checkbox"/>	L7	back pain	3480
<input type="checkbox"/>	L6	L4 and L5	951
<input type="checkbox"/>	L5	radiculopathy or spine or back pain or cervical or lumbar or sacral	48053
<input type="checkbox"/>	L4	L1 and L3	2019
<input type="checkbox"/>	L3	pain with treat\$4	19243
<input type="checkbox"/>	L2	pain with treat\$3	11013
<input type="checkbox"/>	L1	methotrexate	22315

END OF SEARCH HISTORY

=&gt; FIL HOME

COST IN U.S. DOLLARS

SINCE FILE

ENTRY

TOTAL

SESSION

FULL ESTIMATED COST

0.06

0.27

FILE 'HOME' ENTERED AT 11:53:21 ON 16 SEP 2004

=&gt; file reg

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Property values tagged with IC are from the ZIC/VINITI data file  
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STRUCTURE FILE UPDATES: 14 SEP 2004 HIGHEST RN 744786-72-9

DICTIONARY FILE UPDATES: 14 SEP 2004 HIGHEST RN 744786-72-9

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Experimental and calculated property data are now available. For more  
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<http://www.cas.org/ONLINE/DBSS/registryss.html>

=&gt; s methotrexate

L1 101 METHOTREXATE

=&gt; s methotrexate/cn

L2 1 METHOTREXATE/CN

=&gt; d 12

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN

RN 59-05-2 REGISTRY

CN L-Glutamic acid, N-[4-[[[2,4-diamino-6-pteridinyl)methyl]methyamino]benzo  
yl]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Glutamic acid, N-[p-[[[2,4-diamino-6-pteridinyl)methyl]methyamino]benzoyl  
]-, L-(+)- (8CI)

OTHER NAMES:

CN (+)-Amethopterin

CN 4-Amino-10-methylfolic acid

CN 4-Amino-N10-methylfolic acid

CN 4-Amino-N10-methylpteroylglutamic acid

CN Amethopterin

CN Amethopterin

CN Antifolan

CN CL 14377

CN EMT 25299

CN Emtexate

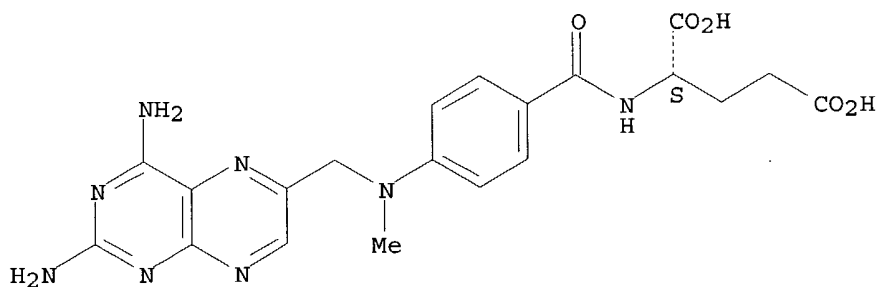
CN L-Amethopterin

CN L-Methotrexate

CN Ledertrexate

CN Metatrexan  
 CN Methotrexat-Ebewe  
 CN **Methotrexate**  
 CN Methylaminopterin  
 CN Mexate  
 CN MTX  
 CN N-[p-[[2,4-Diamino-6-pteridiny]methyl]methylamino]benzoyl]-L-(+)-glutamic acid  
 CN NSC 740  
 CN R 9985  
 CN Rheumatrex  
 FS STEREOSEARCH  
 MF C20 H22 N8 O5  
 CI COM  
 LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, HSDB\*, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IPA, MEDLINE, MRCK\*, MSDS-OHS, NIOSHTIC, PHAR, PROMT, PROUSDDR, PS, RTECS\*, SPECINFO, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL, VETU  
 (\*File contains numerically searchable property data)  
 Other Sources: EINECS\*\*, NDSL\*\*, TSCA\*\*, WHO  
 (\*\*Enter CHEMLIST File for up-to-date regulatory information)  
 DT.CA Caplus document type: Book; Conference; Dissertation; Journal; Patent; Report  
 RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)  
 RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)  
 RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)  
 RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

11312 REFERENCES IN FILE CA (1907 TO DATE)  
 757 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 11349 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
 73 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> file medicine

FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED

COST IN U.S. DOLLARS

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TOTAL

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FULL ESTIMATED COST

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=> s methotrexate  
L3 278691 METHOTREXATE

=> s radiculopathy or spine or back pain or cervical or lumbar or sacral  
25 FILES SEARCHED...

L4 991684 RADICULOPATHY OR SPINE OR BACK PAIN OR CERVICAL OR LUMBAR OR  
SACRAL

=> s l3 and l4  
L5 9736 L3 AND L4

=> s radiculopathy  
L6 10724 RADICULOPATHY

=> s l5 and l6  
L7 93 L5 AND L6

=> s back pain or lumber  
L8 116716 BACK PAIN OR LUMBER

=> s back pain  
L9 87579 BACK PAIN

=> s l7 and l9  
L10 9 L7 AND L9

=> dup rem  
ENTER L# LIST OR (END):l10  
DUPLICATE IS NOT AVAILABLE IN 'ADISINSIGHT, ADISNEWS, DRUGMONOG2, IMSPRODUCT,  
KOSMET, MEDICONF, NUTRACEUT, PCTGEN, PHARMAML'.  
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE  
PROCESSING COMPLETED FOR L10  
L11 9 DUP REM L10 (0 DUPLICATES REMOVED)

=> d l11 1-9 ibib, kwic

L11 ANSWER 1 OF 9 USPATFULL on STN  
ACCESSION NUMBER: 2004:203941 USPATFULL  
TITLE: Pharmaceutical composition of 1- (3,4-dimethoxyphenyl)-  
4-methyl-5-ethyl-7-methoxy-8-hydroxy-5H-2,3-  
benzodiazepine and uses thereof  
INVENTOR(S): Harris, Herbert W., Merion, PA, UNITED STATES  
Kucharik, Robert F., Glenmoore, PA, UNITED STATES  
Leventer, Steven M., Langhorne, PA, UNITED STATES  
PATENT ASSIGNEE(S): Vela Pharmaceuticals, Inc., Lawrenceville, NJ (U.S.  
corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004157833	A1	20040812
APPLICATION INFO.:	US 2003-728261	A1	20031203 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-430771P	20021203 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	DRINKER BIDDLE & REATH, ONE LOGAN SQUARE, 18TH AND CHERRY STREETS, PHILADELPHIA, PA, 19103-6996	
NUMBER OF CLAIMS:	58	
EXEMPLARY CLAIM:	1	
LINE COUNT:	1897	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . of 3-15% of patients, and bone marrow suppression, which  
requires regular monitoring. More potent immunosuppressive drugs such as  
cyclosporine and **methotrexate** have been employed, but toxicity  
of these drugs limits their use to specific situations of refractory  
disease states. Other therapeutic. . .

SUMM . . . can take several weeks or months to demonstrate a clinical

effect. DMARD's include leflunomide (Arava.TM.), etanercept (Enbrel.TM.), infliximab (Remicade.TM.), antimalarials, **methotrexate**, gold salts, sulfasalazine, d-penicillamine, cyclosporin A, cyclophosphamide and azathioprine. Because cartilage damage and bony erosions frequently occur within the first. . .

SUMM . . . rat model examined the role of TXA.sub.2 (and LTB.sub.4) in the hyperalgesia induced by application of nucleus pulposus to the **lumbar** nerve root in the rat. A TXA.sub.2 synthetase inhibitor, injected into the epidural space, decreased mechanical hyperalgesia at both three. . . following application of the nucleus pulposus or an epidural injection. Epidural injection of TXA.sub.2 synthetase inhibitor may attenuate the painful **radiculopathy** due to **lumbar** disc herniation.

DETD . . . hyperalgesia, inflammatory pain, nociceptive pain, tabes dorsalis, phantom limb pain, spinal cord injury pain, central pain, post-herpetic pain, HIV pain, **back pain**, neck pain, dental pain, premenstrual pain, visceral pain, pain due to burns, migraine or cluster headaches, and neuralgias. Thus compositions. . .

L11 ANSWER 2 OF 9 USPATFULL on STN

ACCESSION NUMBER: 2004:120053 USPATFULL  
 TITLE: Method for reducing pain using oncolytic viruses  
 INVENTOR(S): Morris, Donald, Calgary, CANADA  
 Coffey, Matthew C., Calgary, CANADA  
 Thompson, Bradley G., Calgary, CANADA  
 PATENT ASSIGNEE(S): Oncolytics Biotech Inc., Calgary, CANADA (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004091458	A1	20040513
APPLICATION INFO.:	US 2003-431580	A1	20030508 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-378675P	20020509 (60)
	US 2003-443177P	20030129 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	FISH & RICHARDSON P.C., 3300 DAIN RAUSCHER PLAZA, MINNEAPOLIS, MN, 55402	
NUMBER OF CLAIMS:	29	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	1 Drawing Page(s)	
LINE COUNT:	1204	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD [0072] Acute pain may be associated with diagnostic procedures including, for example, **lumbar** puncture, bone marrow biopsy, and paracentesis. Acute pain may be associated with therapeutic procedures including, for example, pleurodesis, tumor embolization, . . .

DETD [0097] The **spine** is the most common site of bone metastases, and **back pain** is an extremely common problem in the cancer population. Any neoplastic lesion of the vertebra has the potential to damage. . . compromise. Specific pain patterns (for example, "crescendo" pain, pain flare with recumbency, or radicular pain), specific neurological findings (for example, **radiculopathy**), and specific radiological findings (for example, 50% collapse of a vertebral body) are suspicious of epidural compression. Epidural spinal cord. . .

DETD . . . intraperitoneally, topically (e.g., for melanoma), orally (e.g., for oral or esophageal neoplasm), rectally (e.g., for colorectal neoplasm), vaginally (e.g., for **cervical** or vaginal neoplasm), nasally or by inhalation spray (e.g., for lung neoplasm).

DETD . . . are compounds which may inhibit the growth of tumors. Such agents, include, but are not limited to, 5-fluorouracil, mitomycin C, **methotrexate**, hydroxyurea, cyclophosphamide, dacarbazine, mitoxantrone, anthracyclins (Epirubicin and Doxorubicin), antibodies to receptors, such as herceptin, etoposide, pregnasome, platinum compounds such as. . .

L11 ANSWER 3 OF 9 USPATFULL on STN

ACCESSION NUMBER: 2003:165464 USPATFULL  
 TITLE: TNF inhibition for the treatment of pre-menstrual syndrome and primary dysmenorrhea  
 INVENTOR(S): Tobinick, Edward Lewis, Los Angeles, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003113318	A1	20030619
APPLICATION INFO.:	US 2003-340890	A1	20030113 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2002-269745, filed on 9 Oct 2002, PENDING Continuation-in-part of Ser. No. US 2002-236097, filed on 6 Sep 2002, PENDING Continuation-in-part of Ser. No. US 2001-841844, filed on 25 Apr 2001, GRANTED, Pat. No. US 6537549 Continuation-in-part of Ser. No. US 2001-826976, filed on 5 Apr 2001, GRANTED, Pat. No. US 6419944 Continuation-in-part of Ser. No. US 2000-563651, filed on 2 May 2000, GRANTED, Pat. No. US 6471961 Continuation-in-part of Ser. No. US 1999-476643, filed on 31 Dec 1999, GRANTED, Pat. No. US 6177077 Continuation-in-part of Ser. No. US 1999-275070, filed on 23 Mar 1999, GRANTED, Pat. No. US 6015557 Continuation-in-part of Ser. No. US 1999-256388, filed on 24 Feb 1999, ABANDONED		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	EZRA SUTTON, P.A., PLAZA 9, 900 ROUTE 9, WOODBRIDGE, NJ, 07095		
NUMBER OF CLAIMS:	6		
EXEMPLARY CLAIM:	1		
LINE COUNT:	795		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . administration involves an anatomically localized injection performed so as to deliver the therapeutic molecule directly into the vicinity of the **spine**. Perispinal administration includes, but is not limited to the subcutaneous, intramuscular, interspinous, epidural, peridural, parenteral, or intrathecal routes, and may. . .

SUMM . . . or, alternatively, to reach the cerebrospinal fluid (CSF). In addition local administration of a biologic in the vicinity of the **spine** (perispinal administration) has the key advantage of improved delivery of the agent to the central nervous system (CNS). Local intranasal. . .

SUMM [0013] Clinical experience utilizing perispinal administration of etanercept for treating **lumbar** and **cervical radiculopathy** and other forms of neuropathic pain caused by vertebral disc disease has demonstrated the dramatic efficacy, and the extraordinarily rapid. . .

SUMM . . . Another object of the present invention is to provide cytokine antagonists, using anatomically localized administration in the vicinity of the **spine** as the preferred forms of administration, that provide therapeutic benefit utilizing either acute or chronic treatment regimens for treating premenstrual. . .

DETD [0033] For the purposes of this discussion, "perispinal" means in the anatomic vicinity of the **spine**. For this discussion "anatomic vicinity" is generally defined as within 10 centimeters, or functionally defined as in close enough anatomic proximity to allow the therapeutic



molecules of consideration herein to reach the **spine** and/or the subarachnoid space surrounding the spinal cord in therapeutic concentration when administered directly to this area. For the treatment.

DETD . . . that administration is simplified. For example, administration for the treatment of an annular tear of an intervertebral disc in the **lumbar spine** is effective by the interspinous route adjacent to the involved disc. This route is simple and safe. Hemorrhage due to.

DETD . . . in the midline, in the interspace between two spinous processes, to deliver the therapeutic molecule in anatomic proximity to the **spine**.

DETD . . . of etanercept, infliximab, CDP 870, D2E7, or onercept in a therapeutically effective dose to the anatomic area adjacent to the **spine**.

DETD . . . of etanercept, infliximab, CDP 870, D2E7, or onercept in a therapeutically effective dose to the anatomic area adjacent to the **spine**, with the dose repeated as a form of chronic therapy at intervals as often as twice per week to as.

DETD [0041] In another preferred embodiment injection of the therapeutic molecule to the anatomic area adjacent to the **spine** is accomplished by interspinous injection.

DETD . . . to be of central importance in the pathogenesis of several types of neuropathic pain, including, but not limited to spinal **radiculopathy**, nerve root inflammation due to intervertebral disc herniation, and neuropathy associated with chronic constriction injury. There are many other forms.

DETD [0067] 7. **Lumbar and Cervical Radiculopathy**

DETD [0068] Inflammation of the nerve roots in the **lumbar** or **cervical** region may lead to neurologic dysfunction. These forms of **radiculopathy** commonly result in pain in a nerve root distribution, often with sensory dysfunction characterized by numbness and/or paresthesia. A smaller.

DETD [0071] 9. **Low Back Pain**

DETD [0072] Low **back pain** (LBP) can result from a wide variety of clinical conditions. Many forms of LBP are mild or spontaneously resolve. Other. . . of TNF antagonists delivered by perispinal administration. In addition this method of treatment has been beneficial for other patients with **back pain**, including those patients with apparently normal MRI examination of the **spine**. Many of these patients may have undiagnosed annular tears of their intervertebral disc capsules, or other forms of internal disc.

DETD [0097] [1]. Bathon J M, Martin R W, Fleischmann R M, et al. A comparison of etanercept and **methotrexate** in patients with early rheumatoid arthritis. N Engl J Med (2000);343:1586-1593.

DETD . . . al. A trial of etanercept, a recombinant tumor necrosis factor receptor: Fc Fusion protein, in patients with rheumatoid arthritis receiving **methotrexate**. N Engl J Med (1999);340(4):253-259.

L11 ANSWER 4 OF 9 USPATFULL on STN

ACCESSION NUMBER: 2003:158984 USPATFULL

TITLE: Application of lipid vehicles and use for drug delivery

INVENTOR(S): Chancellor, Michael B., Pittsburgh, PA, UNITED STATES

Fraser, Matthew O., Apex, NC, UNITED STATES

Chuang, Yao-Chi, Niao-Sung Hsiang, TAIWAN, PROVINCE OF CHINA

de Groat, William C., Pittsburgh, PA, UNITED STATES

Huang, Leaf, Pittsburgh, PA, UNITED STATES

Yoshimura, Naoki, Pittsburgh, PA, UNITED STATES

NUMBER KIND DATE

PATENT INFORMATION: US 2003108597 A1 20030612

APPLICATION INFO.: US 2002-218797 A1 20020813 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-311868P	20010813 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	MORGAN & FINNEGAN, L.L.P., 345 Park Avenue, New York, NY, 10154-0053	
NUMBER OF CLAIMS:	59	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	7 Drawing Page(s)	
LINE COUNT:	2549	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . to be useful in treating the pain and discomfort associated with menstrual cramps, bloating, and/or muscular pain such as muscular **back pain**. Several studies have assessed intravesical capsaicin as a treatment for urge incontinence in patients with spinal detrusor hyperreflexia or bladder. . . .

DETD . . . certain preferred aspects, the bioactive agent will be an antineoplastic agent, such as vincristine, doxorubicin, mitoxantrone, camptothecin, cisplatin, bleomycin, cyclophosphamide, **methotrexate**, streptozotocin, and the like. Especially preferred antitumor agents include, for example, actinomycin D, vincristine, vinblastine, cystine arabinoside, anthracyclines, alkylative agents, platinum compounds, antimetabolites, and nucleoside analogs, such as **methotrexate** and purine and pyrimidine analogs. Anticancer agents further include carcinostatic agents such as adriamycin, daunomycin, mitomycin, epirubicin, 5-FU, and aclacinomycin, . . .

DETD . . . anastomosis; myoclonus of spinal cord origin; voice defects (e.g., stuttering); painful rigidity; tension headaches; lumbosacral strain and back spasm (myofascial); **radiculopathy** with secondary muscle spasm; spasticity; IC, spastic bladder; UDSD; achalasia (esophageal); pelvicorectal spasms (anismus and vaginismus); segmental dystonia, focal dystonia (e.g., blepharospasm (lid apraxia); oromandiibular dystonia, facial dystonia, lingual dystonia, **cervical** dystonia (torticollis) and spasticity; laryngeal dystonia (spasmodic dysphonia; adductor spasmodic dysphonia, and abductor spasmodic dysphonia); task-specific dystonia (occupational cramps, such. . . .

DETD . . . tics, strabismus, nystagmus, eyelid entropion, myokymia, bruxism, tardive dysknetic syndrome, lateral rectus palsy, stuttering, painful rigidity, tension headache, back spasm, **radiculopathy**, spasticity, spastic bladder, urinary detrusor-sphincter dyssynergia, achalasia, anismus, vaginismus, segmental dystonia, idiopathic dystonia, and secondary focal distonia.

DETD . . . contraction is associated with a focal dystonia selected from the group consisting of blepharospasm, oromandiibular dystonia, facial dystonia, lingual dystonia, **cervical** dystonia, torticollis, spasmodic dysphonia, and task-specific dystonia.

CLM What is claimed is:

. . . claim 29, wherein the anticancer agent is selected from the group consisting of vincristine, doxorubicin, mitoxantrone, camptothecin, cisplatin, bleomycin, cyclophosphamide, **methotrexate**, streptozotocin, actinomycin D, vincristine, vinblastine, cystine arabinoside, anthracyclines, alkylative agents, platinum compounds, antimetabolites, nucleoside analogs, **methotrexate**, purine and pyrimidine analogs, adriamycin, daunomycin, mitomycin, epirubicin, 5-FU, and aclacinomycin.

L11 ANSWER 5 OF 9 USPATFULL on STN

ACCESSION NUMBER: 2003:70971 USPATFULL

TITLE: Cytokine antagonists for neurological and

neuropsychiatric disorders  
 INVENTOR(S): Tobinick, Edward Lewis, Los Angeles, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003049256	A1	20030313
APPLICATION INFO.:	US 2002-269745	A1	20021009 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2002-236097, filed on 6 Sep 2002, PENDING Continuation-in-part of Ser. No. US 2001-841844, filed on 25 Apr 2001, PENDING Continuation-in-part of Ser. No. US 2001-826976, filed on 5 Apr 2001, GRANTED, Pat. No. US 6419944 Continuation-in-part of Ser. No. US 2000-563651, filed on 2 May 2000, GRANTED, Pat. No. US 6471961 Continuation-in-part of Ser. No. US 1999-476643, filed on 31 Dec 1999, GRANTED, Pat. No. US 6177077 Continuation-in-part of Ser. No. US 1999-275070, filed on 23 Mar 1999, GRANTED, Pat. No. US 6015557 Continuation-in-part of Ser. No. US 1999-256388, filed on 24 Feb 1999, ABANDONED		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	EZRA SUTTON, ESQ., EZRA SUTTON, P.A., Plaza 9, 900 Route 9, Woodbridge, NJ, 07095		
NUMBER OF CLAIMS:	59		
EXEMPLARY CLAIM:	1		
LINE COUNT:	1305		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB . . . to the following: diseases of the brain, including neurodegenerative diseases such as Alzheimer's Disease and Parkinson's Disease; migraine headache; spinal **radiculopathy** associated with intervertebral disc herniation, post-herpetic neuralgia, reflex sympathetic dystrophy, neuropathic pain, vertebral disc disease, low **back pain**, amyotrophic lateral sclerosis, chronic fatigue syndrome; and neuropsychiatric diseases, including bipolar affective disorder, anorexia nervosa, nicotine withdrawal, narcotic addiction, alcohol. . . .

SUMM . . . but not limited to migraine headaches and cluster headaches; neurologic disorders associated with neuropathic pain, including, but not limited to **lumbar** and **cervical radiculopathy**, low **back pain**, vertebral disc disease, fibromyalgia, post-herpetic neuralgia, and reflex sympathetic dystrophy; and chronic fatigue syndrome; utilizing specific anatomic methods of administration. . . . administration involves an anatomically localized injection performed so as to deliver the therapeutic molecule directly into the vicinity of the **spine**. Perispinal administration includes, but is not limited to the subcutaneous, intramuscular, interspinous, epidural, peridural, parenteral, or intrathecal routes, and may. . . .

SUMM . . . or, alternatively, to reach the cerebrospinal fluid (CSF). In addition local administration of a biologic in the vicinity of the **spine** (perispinal administration) has the key advantage of improved delivery of the agent to the central nervous system (CNS). Local intranasal. . . .

SUMM [0013] Clinical experience utilizing perispinal administration of etanercept for treating **lumbar** and **cervical radiculopathy** and other forms of neuropathic pain caused by vertebral disc disease has demonstrated the dramatic efficacy, and the extraordinarily rapid. . . .

SUMM . . . Another object of the present invention is to provide cytokine antagonists, using anatomically localized administration in the vicinity of the **spine** as the preferred forms of administration, that provide therapeutic benefit utilizing either acute or chronic treatment regimens for treating neurological. . . .

DETD [0033] For the purposes of this discussion, "perispinal" means in the anatomic vicinity of the **spine**. For this discussion "anatomic vicinity" is generally defined as within 10 centimeters, or functionally defined as in close enough anatomic proximity to allow the therapeutic molecules of consideration herein to reach the **spine** and/or the subarachnoid space surrounding the spinal cord in therapeutic concentration when administered directly to this area. For the treatment. . . .

DETD . . . . that administration is simplified. For example, administration for the treatment of an annular tear of an intervertebral disc in the **lumbar spine** is effective by the interspinous route adjacent to the involved disc. This route is simple and safe. Hemorrhage due to. . . .

DETD . . . . in the midline, in the interspace between two spinous processes, to deliver the therapeutic molecule in anatomic proximity to the **spine**.

DETD . . . . of etanercept, infliximab, CDP 870, D2E7, or onercept in a therapeutically effective dose to the anatomic area adjacent to the **spine**.

DETD . . . . of etanercept, infliximab, CDP 870, D2E7, or onercept in a therapeutically effective dose to the anatomic area adjacent to the **spine**, with the dose repeated as a form of chronic therapy at intervals as often as twice per week to as. . . .

DETD . . . . of etanercept, infliximab, CDP 870, D2E7, or onercept in a therapeutically effective dose to the anatomic area adjacent to the **spine** with a single dose administered 48 hours after beginning a course of antiviral medication.

DETD [0042] In another preferred embodiment a patient with **lumbar radiculopathy** due to an intervertebral disc herniation is treated by injection of a IL-1 antagonist selected from the group of IL-1. . . .

DETD [0043] In another preferred embodiment injection of the therapeutic molecule to the anatomic area adjacent to the **spine** is accomplished by interspinous injection.

DETD [0045] An example of one preferred embodiment for treatment of **lumbar radiculopathy** due to disc herniation at the L 3-4 interspace is the perispinal administration of etanercept 25 mg by injecting through. . . .

DETD . . . . to be of central importance in the pathogenesis of several types of neuropathic pain, including, but not limited to spinal **radiculopathy**, nerve root inflammation due to intervertebral disc herniation, and neuropathy associated with chronic constriction injury. There are many other forms. . . .

DETD [0089] 15. **Lumbar And Cervical Radiculopathy**

DETD [0090] Inflammation of the nerve roots in the **lumbar** or **cervical** region may lead to neurologic dysfunction. These forms of **radiculopathy** commonly result in pain in a nerve root distribution, often with sensory dysfunction characterized by numbness and/or paresthesia. A smaller. . . .

DETD [0093] 17. **Low Back Pain**

DETD [0094] Low **back pain** (LBP) can result from a wide variety of clinical conditions. Many forms of LBP are mild or spontaneously resolve. Other. . . . of TNF antagonists delivered by perispinal administration. In addition this method of treatment has been beneficial for other patients with **back pain**, including those patients with apparently normal MRI examination of the **spine**. Many of these patients may have undiagnosed annular tears of their intervertebral disc capsules, or other forms of internal disc. . . .

DETD . . . . the extradiscal space. This may result in TNF-mediated neurotoxicity, inflammation, and resulting neuropathic pain and/or sensory and motor neuropathy or **radiculopathy**. These patients may have frank disc herniation, or more subtle forms of disc disruption, such as disc bulging, disc protrusion,. . . .

DETD . . . localized administration, including perispinal administration, as the preferred form of administration, for the treatment of neurological disorders, including dementia, low **back pain**, and neuropathic pain.

DETD [0122] [1]. Bathon J M, Martin R W, Fleischmann R M, et al. A comparison of etanercept and **methotrexate** in patients with early rheumatoid arthritis. N Engl J Med (2000);343:1586-1593.

DETD . . . et al. A trial of etanercept, a recombinant tumor necrosis factor receptor:Fc Fusion protein, in patients with rheumatoid arthritis receiving **methotrexate**. N Engl J Med (1999);340(4):253-259.

CLM What is claimed is:

. . . the action of TNF in accordance with claim 11, wherein the step of administering said dosage level is for treating **lumbar** or **cervical radiculopathy**.

41. A method for treating low **back pain** in a human by inhibiting the action of tumor necrosis factor (TNF) through the administration of a TNF antagonist comprising. . .

45. A method for treating low **back pain** in a human by inhibiting the action of tumor necrosis factor (TNF) through the administration of a TNF antagonist comprising. . .

L11 ANSWER 6 OF 9 USPATFULL on STN

ACCESSION NUMBER: 2003:10278 USPATFULL

TITLE: Cytokine antagonists and other biologics for the treatment of bone metastases

INVENTOR(S): Tobinick, Edward, Los Angeles, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003007972	A1	20030109
APPLICATION INFO.:	US 2002-236097	A1	20020906 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2001-841844, filed on 25 Apr 2001, PENDING Continuation-in-part of Ser. No. US 2001-826976, filed on 5 Apr 2001, GRANTED, Pat. No. US 6419944 Continuation-in-part of Ser. No. US 2000-563651, filed on 2 May 2000, GRANTED, Pat. No. US 6471961 Continuation-in-part of Ser. No. US 1999-476643, filed on 31 Dec 1999, GRANTED, Pat. No. US 6177077 Continuation-in-part of Ser. No. US 1999-275070, filed on 23 Mar 1999, GRANTED, Pat. No. US 6015557 Continuation-in-part of Ser. No. US 1999-256388, filed on 24 Feb 1999, ABANDONED		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	Ezra Sutton, P.A., Plaza 9, 900 Route 9, Woodbridge, NJ, 07095		
NUMBER OF CLAIMS:	22		
EXEMPLARY CLAIM:	1		
LINE COUNT:	913		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM [0012] The inventor's extensive clinical experience utilizing local administration of etanercept for treating **lumbar** and **cervical radiculopathy** has demonstrated the dramatic efficacy, and the extraordinarily rapid onset of action produced by perilesional administration of etanercept for these. . .

SUMM . . . bone from cancers with primary lesions distant from the sites of bone destruction. Many cancers can metastasize to bone. The **spine** and ribs are among the most common sites of metastasis. Both of these sites are amenable to therapeutic intervention utilizing.

DETD . . . method of delivery is that administration is simplified. For example, administration for the treatment of a bone metastasis to the **lumbar spine** is effective by the interspinous route

adjacent to the involved vertebrae. This route is simple and safe. Hemorrhage due to. . .

- DETD . . . anatomic proximity to the site of the pathologic process being treated; perispinal is defined as in anatomic proximity to the **spine**; and peridural is defined as in anatomic proximity to the dura of the spinal cord. Perilesional is used generally to. . .
- DETD . . . obtained may be useful, as well as physical examination, which will usually reveal localized areas of tenderness. Metastases to the **spine** and ribs are usually accessible. The biologic, in a therapeutically effective dose, can then be administered to a site anatomically. . .
- DETD [0043] In one preferred embodiment a patient with cancer metastatic to a **lumbar** vertebrae complaining of severe persistent pain is treated by injection of a TNF antagonist selected from the group of etanercept,. . .
- DETD [0044] In another preferred embodiment a patient with cancer metastatic to a **lumbar** vertebrae complaining of severe persistent pain is treated by injection of a IL-1 antagonist selected from the group of IL-1. . .
- DETD [0045] In another preferred embodiment a patient with cancer metastatic to a **lumbar** vertebrae complaining of severe persistent pain is treated by injection of osteoprotegerin in a therapeutically effective dose to the anatomic. . .
- DETD . . . accomplished by injection through the skin and through the interspinous ligament, either immediately above or immediately below the site of **spine** metastasis.
- DETD [0048] An example of one preferred embodiment for treatment of a breast cancer metastasis to the fourth **lumbar** vertebrae is the perilesional injection of etanercept 25 mg by injecting through the skin of the back, carried through the. . .
- DETD . . . interfere with TNF-mediated bone destruction, etanercept was administered to two patients with treatment-refractory pain due to cancer metastasis to the **spine**.
- DETD [0064] Patient 1.--A 77 y.o. Caucasian woman began having severe and unrelenting mid-**back pain** in January 2001. In May 2001 she developed a dry, unproductive cough. In July 2001 a rapidly growing nodule appeared. . . the lung. Bone scan in August 2001 showed intense focal areas of increased uptake involving the right frontal skull and **spine** at T11. Plain x-rays of the back showed a metastatic lesion of the T11 vertebrae, with compression fracture and destruction. . . of radiation to her right forehead lesion, and a single course of radiation to T11 in September, but severe, unrelenting **back pain** continued. The patient was prescribed fentanyl patches and morphine, which she required daily throughout August and September, but pain control. . . ambulating due to the pain, and could not exit or enter an automobile without assistance. In October, ten months after **back pain** began, the patient presented to our office for treatment of the localized mid-**back pain** which was constant, present 24 hours per day, and despite multiple daily doses of morphine was not adequately controlled. After. . .
- DETD . . . was treated with lumpectomy and radiation therapy. Four years later she developed bilateral hip pain and several months later low **back pain** began. Bone scan showed increased uptake in the ischium, ribs, and **lumbar spine** at L4. The patient underwent left hip reconstruction and replacement due to metastatic disease. Biopsy specimens from the hip surgery. . . inadequate. One month prior to her visit to our office a PET scan documented increased metabolic activity in the lower **lumbar spine** at L4 and in a lower right rib, consistent with bone metastases. The patient presented to our office for treatment of intractable low **back pain** of two years duration and was able to ambulate only with the use of crutches due to pathologic fractures involving both hips. The low **back pain** at

the site of spinal metastasis at L4 was constant, present 24 hours per day for more than two years. Informed consent was obtained. Etanercept (Enbrel®, Immunex) 25 mg by subcutaneous injection was administered to the **lumbar** area.

DETD . . . in rapid, substantial, and prolonged relief of previously treatment-refractory pain in each of these patients with cancer metastatic to their **spine**.

DETD . . . appetite, and the ability to get into or out of a car without assistance. At one month complete relief of **back pain** continued. At five weeks moderately severe mid-**back pain** returned, accompanied by difficulty rising out of a chair without assistance, and a second dose of etanercept 25 mg subcutaneously was administered. One day after the second dose pain relief began. After two days relief of **back pain** was complete, and she experienced no further **back pain** for the rest of her life, which lasted an additional five months until death ensued from extension of the right. . . .

DETD . . . treatment. At five weeks following the single dose of etanercept the patient continued to report 90% relief of her lower **back pain**. Immediately following treatment the patient was able to decrease her pain medication significantly. Oswestry Pain Disability score[8]prior to treatment was. . . .

DETD [0096] [5]. Bathon J M, Martin R W, Fleischmann R M, et al. A comparison of etanercept and **methotrexate** in patients with early rheumatoid arthritis. N Engl J Med (2000);343:1586-1593.

DETD [0099] [8]. Fairbank J, Davies J, Coupar J, O'Brien J P. The Oswestry low **back pain** disability questionnaire. Physiotherapy (1980);66:271-3.

DETD . . . et al. A trial of etanercept, a recombinant tumor necrosis factor receptor:Fc Fusion protein, in patients with rheumatoid arthritis receiving **methotrexate**. N Engl J Med (1999);340(4):253-259.

L11 ANSWER 7 OF 9 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2001:423277 BIOSIS

DOCUMENT NUMBER: PREV200100423277

TITLE: **Sacral radiculopathy** secondary to multicentric osteosarcoma.

AUTHOR(S): Yamamoto, Tetsuji [Reprint author]; Fujita, Ikuo; Kurosaka, Masahiro; Mizuno, Kosaku

CORPORATE SOURCE: Department of Orthopaedic Surgery, Kobe University School of Medicine, 7-5-1 Kusunoki-cho, Chuo-ku, Kobe, 650-0017, Japan

SOURCE: yamatetu@med.kobe-u.ac.jp  
Spine, (August 1, 2001) Vol. 26, No. 15, pp. 1729-1732.  
print.

CODEN: SPINDD. ISSN: 0362-2436.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 5 Sep 2001

Last Updated on STN: 22 Feb 2002

TI **Sacral radiculopathy** secondary to multicentric osteosarcoma.

AB Study Design: A case of multicentric osteosarcoma presenting with **sacral radiculopathy** is reported. Objective: To present unusual clinical and radiologic findings of multicentric osteosarcoma. Summary of Background Data: Multicentric osteosarcoma is a rare variant of osteosarcoma. To the authors' knowledge, no cases of multicentric osteosarcoma presenting as **sacral radiculopathy** have been reported previously. Methods: A 14-year-old boy had a large **sacral** tumor extending into the spinal canal, which was found to account for the initial symptoms, which mimicked those of herniated. . . . after the initial presentation. Conclusion: Multicentric osteosarcoma should be considered in the differential diagnosis for a pediatric patient with low **back pain** and sciatica.

IT . . .

## Diseases

osteosarcoma: bone disease, neoplastic disease, clinical presentation, differential diagnosis, histopathology, metastasis, multicentric, treatment

Bone Neoplasms (MeSH); Osteosarcoma (MeSH)

IT Diseases

**sacral radiculopathy**: bone disease, comorbidity, diagnosis

IT Chemicals &amp; Biochemicals

**methotrexate**-doxorubicin-cisplatin: antineoplastic-drug

L11 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:401641 CAPLUS

DOCUMENT NUMBER: 133:12774

TITLE: An animal model for chronic pain and compounds identified via this model for treatment of chronic pain

INVENTOR(S): Deleo, Joyce A.; Weinstein, James N.

PATENT ASSIGNEE(S): Trustees of Dartmouth College, USA

SOURCE: PCT Int. Appl., 20 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000033830	A1	20000615	WO 1999-US25187	19991028
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

PRIORITY APPLN. INFO.: US 1998-111181P P 19981207  
US 1999-147442P P 19990805

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB An animal model for chronic pain, and in particular lower **back pain**, is provided. Methods of identifying agents and reducing chronic pain with identified agents, e.g. **methotrexate**, are also provided.

ST chronic pain animal model analgesic screening; lower **back pain** animal model analgesic screening; **methotrexate** chronic pain treatment animal model

IT Body, anatomical  
(**back, pain**, lower back; animal model for chronic pain and compds. identified by this model for treatment of chronic pain)

IT Spinal cord  
(injury, **lumbar** root injury; animal model for chronic pain and compds. identified by this model for treatment of chronic pain)

IT Spinal cord  
(**lumbar**, L5 spinal root; animal model for chronic pain and compds. identified by this model for treatment of chronic pain)

IT Nerve, disease  
(**radiculopathy**; animal model for chronic pain and compds. identified by this model for treatment of chronic pain)

IT 59-05-2, **Methotrexate**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(animal model for chronic pain and compds. identified by this model for treatment of chronic pain)



L11 ANSWER 9 OF 9 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on  
STN

ACCESSION NUMBER: 2000:642983 SCISEARCH

THE GENUINE ARTICLE: 345KA

TITLE: Central administration of **methotrexate** reduces  
mechanical allodynia in an animal model of  
**radiculopathy**/sciatica

AUTHOR: Hashizume H; Rutkowski M D; Weinstein J N; DeLeo J A  
(Reprint)

CORPORATE SOURCE: DARTMOUTH HITCHCOCK MED CTR, DEPT ANESTHESIOLOGY, HINMAN BOX  
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CTR, DEPT ANESTHESIOLOGY, LEBANON, NH 03756; DARTMOUTH  
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DARTMOUTH COLL SCH MED, DEPT COMMUNITY & FAMILY MED,  
HANOVER, NH 03755; DARTMOUTH COLL, DEPT PHARMACOLOGY,  
HANOVER, NH 03755

COUNTRY OF AUTHOR: USA

SOURCE: PAIN, (AUG 2000) Vol. 87, No. 2, pp. 159-169.  
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE  
AMSTERDAM, NETHERLANDS.  
ISSN: 0304-3959.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE; CLIN

LANGUAGE: English

REFERENCE COUNT: 44

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

TI Central administration of **methotrexate** reduces mechanical  
allodynia in an animal model of **radiculopathy**/sciatica

AB We have recently reported that injury to a **lumbar** root in a  
rat model of **radiculopathy** produces spinal glial activation  
associated with elevated proinflammatory cytokines. Based on our  
hypothesis that central neuroinflammatory processes may manifest  
clinically as radicular pain, we undertook pharmacological intervention  
using the immunosuppressive agent **methotrexate** (MTX). The L5  
**lumbar** spinal root (central to the dorsal root ganglia) was  
exposed unilaterally and loosely constricted with chromic gut. In the  
prevention.

ST Author Keywords: **methotrexate**; nerve root; **radiculopathy**  
; chronic pain

STP KeyWords Plus (R): LOW-BACK-PAIN; PORCINE  
CAUDA-EQUINA; RHEUMATOID-ARTHRITIS; NUCLEUS PULPOSUS; NERVE INJURY;  
SPINAL-CORD; T-CELLS; IN-VIVO; RAT; ACTIVATION